REMARKS

All the claims submitted for examination in this application have been objected to or rejected. Applicants have amended their claims and respectfully submit that all the claims currently in this application are patentable over the objection and rejection of record.

Four formal grounds of rejection are imposed in the outstanding Official Action. The first of these, embodied in Paragraph 1 of the Detailed Action, is directed to Claims 1 to 4 and 6 to 15. These claims stand rejected, under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

Specifically, this ground of rejection is predicated on the alleged absence in the specification of description of the subject matter of the rejected claims to enable one skilled in the art to make and use the invention. That is, the Official Action avers that Claims 1 to 4 and 6 to 15 do not meet the test of enablement set forth in In re Wands, 853 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546 (PTO Bd. App. 1986).

Suffice it to say, the authorities relied upon in support of this ground of rejection hold that enablement of a claimed invention is not provided when the amount of experimentation needed is unduly extensive. However, these cases do not deny that enablement is not precluded even if some experimentation is necessary. The test is whether the amount of experimentation necessary is not unduly extensive. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F2d 1367, 231 USPQ 81 (Fed. Cir. 1986, cert. denied 480 U.S. 947(1987).

In the present application Claims 1-4, 6 and 7 are deemed not enabled insofar as the generic formula of Claim 1 is exemplified only for the case where m is 2; o is 1 and n is 1. Thus, the embodiments of the generic formula where m is 1; o is 2 and n is 2 are not exemplified.

To begin with, it is noted that half of the meanings of the radicals within the scope of these three radicals are exemplified. Applicants submit that exemplification of half the meanings of the radicals is sufficient to enable those skilled in the art to make and use all members having the claimed meanings of m, o and n.

Even more significant is the fact that the methods of manufacture, set forth in the specification by Schemes 1 to 5, which represent all the methods employed in manufacturing the compounds of the present application, all utilize a generic formula wherein m, n and o can be utilized with any of the meanings of these terms. It is thus apparent that, independent of the meanings of the subscripts, the illustration of any one of them applies to all the others. As such, no experimentation is necessary given the scope of disclosure in the specification, to make and use the compounds having the meanings of m, o and n not exemplified in the specification. As such, this ground of rejection is respectfully submitted to be without merit.

The remaining claims subject to this formal ground of rejection, Claims 9, 11, 13 and 15, are directed to a method of treating schizophrenia or a condition which is responsive to the activity of α-7 nicotinic receptor modulators. The Official Action argues that the specification provides no definitive evidence to correlate any disorder recited in the claims with the claimed diazabicyclo derivatives.

Three of the factors mentioned in Wands in evaluating the enablement issue are the state of the prior art; the predictability or lack thereof in the art; and the quantity of experimentation needed. Where the state of the art indicates the predictability of certain activity and thus limits the quantity of experimentation needed, the specification, although not including working examples, may suffice to meet the enablement requirement.

So it is in the present application. Many references are recited in the specification establishing that α-7 nicotinic receptor agonists are therapeutic in the treatment of schizophrenia and other central nervous system disorders. Insofar as the compounds recited in the claims subject to this ground of rejection include an α-7 nicotinic receptor agonist it is apparent that the state of the art predicts the recited activity and it is thus unnecessary that there be working examples establishing that utility. Therefore, this formal ground of rejection is submitted to be unsustainable.

A second related formal ground of rejection is embodied in Paragraph 2 of the Detailed Action. That paragraph rejects Claims 12 to 15, under 35 U.S.C. §112, first paragraph, as containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This narrow ground of rejection focuses upon treatment of chemical dependencies and addictions. The Official Action makes blanket statements to the effect that no compound can be used to treat drug addiction. The basis for this allegation is that drug addiction is a collection of diseases that have little in common.

The blanket statement made in Paragraph 2 cannot be justified since it contains facts not in evidence. No support is provided to sustain the argument made in Paragraph 2 that addiction to various addictive substances, such as barbiturates, alcohol, cocaine, opiates, amphetamines, benzodiazepines, nicotine and the like, cannot be treated with a single class of compounds.

Indeed, in contradiction to this argument, applicants submit that many drugs have been patented for treatment of mental disorders which involve more than one portion of the brain.

Therefore, in the absence of such evidence, which is not proffered in the present Official Action, this ground of rejection is unsustainable.

Yet a third formal ground of rejection, also directed to enablement, resides in the rejection of Claims 12 to 15, under 35 U.S.C. §112, first paragraph, as not being enabled.

This ground of rejection, embodied in Paragraph 3 of the Detailed Action, is indeed puzzling. The Official Action, in advancing this ground of rejection, admits that recent studies indicate that many mental diseases, such as senile dementia of the Alzheimer's type, Parkinson's disease, Huntington's Chorea, tardive dyskinesia, hyperkinesia, mania, depression, attention deficit disorder, anxiety, dyslexia, schizophrenia, Tourette's syndrome and addiction to smoking, are conditions that are associated with α-7 nicotinic receptors.

The crux of this ground of rejection is that many of these diseases are difficult to cure. The Official Action therefore concludes that any non-traditional method of treatment is not enabled. In effect, the Official Action bars any patentable advance insofar as that patentable invention is new and previous attempts at treating these conditions have not been fully successful. Such an analysis is inimical to the patent system. This ground of rejection is nothing more than an allegation that anything that is new is not enabled.

This ground of rejection, furthermore, is merely the Examiner's opinion and there is nothing stated in Paragraph 3 which supports the contention that Claims 12 to 15 are not enabled by the specification. In the absence of proof, supplied by the Examiner, of non-operability, this argument in support of non-enablement does not make unpatentable any of Claims 12 to 15 under 35 U.S.C. §112, first paragraph.

Paragraph 4 of the Detailed Action sets forth the fourth formal ground of rejection imposed in the outstanding Official Action. This ground of rejection is directed to all the

claims currently in this application, Claims 1-20. It is noted in passing that this is inconsistent with the outstanding Office Action Summary, wherein it is recited that only Claims 1 to 18 and 20 are rejected and that Claim 19 is objected to. Indeed, there is no specific objection included in the Detailed Action.

Be that as it may, Claims 1 to 20 stand rejected, under 35 U.S.C. §112, second paragraph, as being indefinite for failure to particularly point out and distinctly claim the subject matter which applicants regard as their invention. Twenty-nine grounds are specifically set forth in support of this ground of rejection. Applicants address each of these separate grounds in the remarks below.

The first ground of indefiniteness, denoted as subparagraph (a), is directed to Claims 1 to 15. These claims are deemed indefinite because one of the definitions of each of R^6, R^7 and R^8 is "(5-12 membered heteroaryl." The absence of a close parenthesis from this moiety makes these claims indefinite.

Applicants have amended Claim 1 wherein this definition of each of R^6, R^7 and R^8 is corrected by removing the parenthesis before "5" and thus eliminating this ground of rejection.

The second ground of rejection, embodied in subparagraph (b), is very similar to the first ground of rejection. In this ground of rejection the meaning "(5-11 membered heterobicycloalkyl" of R^9, R^{10} and R^{11} is provided. The absence of a close parenthesis makes this an indefinite term.

Applicants have amended Claim 1 wherein this definition of each of R^9, R^{10} and $R^{11}$is corrected by eliminating the parenthesis before "5" to thus eliminate this ground of rejection.

Subparagraph (c) is directed to Claim 16. Claim 16 is deemed indefinite in that many of the definitions of Q are redundant with definitions of R^3. Thus, there is double inclusion of many of the meanings of Q.

To overcome this ground of rejection, Claim 6 has been amended to eliminate, as one of the meanings of Q, the meaning R^3. The absence of R^3 eliminates any double inclusion of definitions of R^3 which overlap definitions of Q set forth in original Claim 6.

Subparagraph (d) is directed to Claims 10, 12 and 14. These claims, directed to pharmaceutical compositions, are deemed substantial duplicates of Claim 8. That is, the Official Action argues that a pharmaceutical composition for the treatment of schizophrenia, which comprises an amount of the compound of Claim 1 effective in treating schizophrenia, is identical to a pharmaceutical composition for the treatment of schizophrenia wherein the amount of the compound of Claim 1 is an α-7 nicotinic receptor agonizing amount of that compound.

The Official Action applied authority in holding that Claims 10, 12 and 14 are identical with Claim 8 is In re Tuominen, 671 F.2d 1359, 213 USPQ 89 (CCPA 1982). Tuominen stands for the proposition that the patentability of a known composition cannot be predicated solely on a claimed preamble setting forth a use for the composition that is not suggested by the prior art.

The principle in Tuominen, is not the same as stating that a preamble in a claim reciting a first use is identical to another claim setting forth a second use.

In any event, the exact concentration of an effective amount of a schizophrenia treating compound of Claim 1 is not necessarily identical with a composition which employs the same compound to provide an α-7 nicotinic receptor agonizing amount of that compound.

Admittedly, the two compounds are directed to the same patentable invention. However, the concentration of the compound of Claim 1 in the pharmaceutical composition of Claim 8 is not necessarily identical with the concentration of compound of Claim 1 in the pharmaceutical composition of Claim 10 useful in providing an α-7 nicotinic receptor agonizing amount of the compound.

The same argument is submitted for the proposition that Claims 12 and 14 are not identical. Claims 12 and 14 are directed to pharmaceutical compositions for the treatment of a disorder or condition recited in a Markush group of a multiplicity of disorders which, it should be emphasized, does not include schizophrenia. The difference between these two claims is that in Claim 12 the amount of the compound of Claim 1 employed is an amount effective in treating those disorders or conditions. In Claim 14 the amount of the compound of Claim 1 included in the composition is the amount necessary to provide an α-7 nicotinic receptor agonizing amount of the compound. These two concentrations are not necessarily identical.

It goes without saying that neither Claim 12 or 14 is identical with Claim 8 or 10 given the fact that the amount of compound of Claim 1 required for the treatment of the disorders of these claims is hardly likely to be identical with that required to treat schizophrenia or an α-7 nicotinic receptor agonizing amount of that compound.

In this regard it is noted that Claims 12 and 14 have been amended. However, these amendments has been made to correct improper Markush group claim language included therein. Indeed, Claims 1, 6, 7, 13 and 15-18 have also been amended to correct improper Markush group claim language.

Subparagraph (e) is directed to Claims 12-15 for the inclusion of the phrase "e.g.". This phase renders the claims indefinite because it is unclear whether the limitation following the phrase are part of the claimed invention.

Applicants have amended Claims 12 to 15 to remove the offending phrase. It is noted that applicants have additional deleted initials for certain of the disorders enumerated in these claims. These non-substantive amendments, as is the case of the aforementioned Markush group claim language amendment, does not affect the scope of the amended claims.

Subparagraph (f) is directed to Claim 16 which is deemed indefinite in that it is not known what is meant by "carbothioic" at Line 27 of page 59.

Applicants submit herewith Page 212 of Hawley's Condensed Chemical Dictionary, 14th Edition. On that page the term "carbothioic" is defined as a suffix denoting an organic acid in which an atom of sulfur replaces an atom of oxygen. As such, this term has a definitive chemical meaning which rebuts any suggestion that this term is indefinite.

Subparagraph (g) is also directed to the same compound which includes the term "carbothioic" in Claim 16. That is, the Official Action questions the meaning of the phrase "O-phenyl ester." Those skilled in the art are aware that this phrase is directed to a phenyl ester radical bonded to an oxygen atom which is bonded to the remainder of the recited compound. In this case the oxygen atom is bonded to Y of formula I.

The next nineteen grounds of indefiniteness, denoted as subparagraphs (h) to (z) of Paragraph 4 of the Detailed Action, are each directed to phrases included in species within the scope of Claim 17. In each case the Official Action avers that there is insufficient antecedent basis for the quoted limitations of these subparagraphs.

Suffice it to say, each of these phrases are part of a compound recited in Claim 17. Insofar as each of these compounds are recited in the specification, and include the objected to phrase of each of these subparagraphs, it is apparent that there is indeed sufficient antecedent basis to support these limitations of the compounds of Claim 17.

In order to limit the length of applicants' remarks, applicants have prepared a Table reciting the subparagraph, the phrase for which there allegedly is unsufficient basis and the example number in the specification of the compound which includes the phrase. Insofar as each of these phrases of each of the compounds are recited in the specification there is obviously sufficient antecedent basis to support the language of each of the compounds recited in Claim 17.

The Table is as follows:

Subparagraph	Limitation	Example No. in the Specification
(h)	Bromo-phenyl	2
(h)	Bromo-phenyl	33
(i)	Cyano-phenyl	21
(j)	Iodo-phenyl	26
(j)	Iodo-phenyl	35
(j)	Iodo-phenyl	53
(k)	Methoxy-phenyl	71
(k)	Methoxy-phenyl	74
(l)	Tert-butyl-phenyl	29
(l)	Tert-butyl-phenyl	50
(m)	Trifluoromethyl-phenyl	32
(m)	Trifluoromethyl-phenyl	42
(n)	Chloro-phenyl	34
(n)	Chloro-phenyl	46
(o)	Cyano-biphenyl	36
(o)	Cyano-biphenyl	87
(p)	Bromo-biphenyl	37
(q)	Fluoro-phenyl	4
(r)	Phenoxy-phenyl	31
(s)	Methyl-biphenyl	79
(s)	Methyl-biphenyl	82
(t)	Chloro-biphenyl	80
(t)	Chloro-biphenyl	83
(t)	Chloro-biophenyl	84
(u)	Methoxy-biphenyl	94
(v)	Biphenyl	57
(w)	Bromo-dimethyl-phenyl	59
(x)	Bromo-methyl-phenyl	60
(y)	Bromo-chloro-phenyl	61
(z)	Dimethyl-phenyl	62

Subparagraph (aa) is directed to the alleged insufficient antecedent basis for the three compounds recited in Claim 18. This rejection is couched in terms of the meaning of the limitation "dimethyl-biphenyl" in the species of that claim. Suffice it to say, the species of Claim 18 are supported in the specification by Examples 71, 86 and 88.

The final ground alleged for insufficient antecedent basis is directed to the compound recited in Claim 20. That ground of rejection is couched, in Subparagraph (ab), as providing an alleged insufficient antecedent basis for the limitation "bromo-phenyl" of the species of that claim. This ground of rejection is made moot by the disclosure in the specification of Compound 2.

The last basis for indefiniteness is encompassed by Subparagraph (ac). That subparagraph rejects Claims 9, 11, 13 and 15 as being vague and indefinite insofar as these claims are directed to the use of the compound of Claim 1 without providing any steps in determining which are the disorders capable of being treated by modulating the activity of the α-7 nicotinic receptor.

The first two of these rejected claims, Claims 9 and 11, recite a method of treating schizophrenia. The third and fourth of these claims, Claims 13 and 15, set forth a method of treating diseases and conditions recited therein. In all four claims this method includes the step of administering to a mammal an amount of the compound according to Claim 1 effective in treating the disorder or condition or an amount of the compound that provides an α-7 nicotinic receptor agonizing amount of the compound so that the disorder may be treated.

Applicants do not appreciate how these claims are indefinite. The questioning of whether a given disease responds or does not respond to the compound is not the province of the examiner. The examiner must accept the recitation of the invention. If the Official Action questions operability, it is incumbent upon the examiner to produce references or proof establishing the inoperability of the claimed compounds in the treatment of the diseases recited in these claims. The speculation discussed in more than two complete pages does nothing to support a rejection predicated upon indefiniteness.

Clearly, nothing in any of these four claims is indefinite. One skilled in the art, indeed even one unskilled in the art, would have no difficulty in understanding the definitiveness of these claims. The basis for this ground of rejection is the alleged ineffectiveness of the compound of Claim 1 in treating the diseases recited to be treatable in these claims. This is, this ground of rejection is predicated upon alleged inoperativeness. The absence of any proof of inoperativeness overcomes this ground of rejection.

Two substantive grounds of rejection are imposed in the outstanding Official Action. The first of these, encompassed in Paragraph 5 of the Detailed Action, is directed to Claims 1-3, 5, 6 and 8-15. These claims stand rejected, under 35 U.S.C. §102(a), as being anticipated by International Publication WO 00/58311 to Gallet et al.

The Official Action states that the Gallet et al. reference teaches compounds, compositions and methods of use of the compounds that meet the language of the rejected claims when Q is formula I is 4-nitrophenyl. This is so insofar as Example 6 of Gallet et al. meets the scope of formula I of Gallet et al, is NO_2.

To overcome this ground of rejection, Claim 1 has been amended to delete the meaning of nitro as a substituent R^2 of Q. Consistent with this amendment, Claim 6 has been amended to delete nitro from the list of substituents for the sole meaning of Q of that claim, (C_6-C_{11}) aryl. Similarly, Claim 16 has been amended to delete the compounds 1,4-diaza-bicyclo[3.2.2]nonane-4-carboxylic acid 4'-nitro-biphenyl-4-yl-ester; 1,4-diaza-bicyclo[3.2.2]nonane-4-carboxylic acid 2'nitro-biphenyl-4-yl-ester; 1,4-diaza-bicyclic[3.2.2]-4-carboxylic acid 3-nitro-phenyl ester; and 1,4-diaza-bicyclo[3.2.2]nonane-4-carboxylic acid 3'-nitro-biphenyl-4-yl ester. As such, the amendments to Claims 6 and 16 provide proper antecedent basis for these claims which each depend from Claim 1.

The second substantive ground of rejection is directed to Claims 1-3. Claims 1-3 stand rejected, under 35 U.S.C. §102(b), as being anticipated by U.S. Patent 3,954,766 to Henry et al.

The outstanding Official Action rejects Claims 1-3 over Henry et al. as anticipating compounds where the compound of Formula I of the present application has the meanings m is 1; n is 1; o is 1; X is oxygen; Y is oxygen or NR^1, where R^1 is ethyl; and Q is ethyl.

The second substantive ground of rejection has been made moot by the amendment to Claim 1 wherein the meaning "straight chain or branched (C_1-C_8) alkyl" has been deleted. As amended, Henry et al. is outside the scope of the Claims 1 to 3 of the present application.

In view of this amendment to Claim 1, Claim 16, which depends from Claim 1, has been further amended to remove three of the compounds originally included therein. These compounds, 1,4-diaza-bicyclo[3.2.2]nonane-4-carboxylic acid methyl ester; 1,4-diaza-bicyclo[3.2.2]nonane-4-carboxylic acid isobutyl ester; and 1,4-diaza-bicyclo[3.3.3]nonane-4-carboxylic acid octyl ester are no longer within the scope of the generic formula of Claim 16, from which Claim 1 depends and thus been cancelled..

The above amendment and remarks establish the patentable nature of all the claims currently in this application. Notice of Allowance and passage to issue of these claims,

Claims 1-20, is therefore respectfully solicited.

Respectfully submitted,

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